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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/555,061

10/28/2005

Hamed Aissaoui

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07/09/2008

DICKSTEIN SHAPIRO LLP

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EXAMINER

MURRAY, JEFFREY H

ART UNIT

PAPER NUMBER

1624

MAIL DATE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/555,061	<b>Applicant(s)</b> AISSAOUI ET AL.	
	<b>Examiner</b> JEFFREY H. MURRAY	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5, 8, 9 and 11-14 is/are pending in the application.
- 4a) Of the above claim(s) 8, 9, 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/28/2005</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. This action is in response to a restriction election filed on May 1, 2008.

There are fourteen claims pending and seven claims under consideration.

Claims 8, 9, 13, and 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 6, 7, and 10 are cancelled. Election was made **without** traverse in the reply filed on May 1, 2008. This is the first action on the merits. The present invention relates to novel quinoxalin-3-one derivatives of the general formula (I) and their use as pharmaceuticals.

### ***Priority***

2. This application is a non-provisional application 10/555,061, filed October 28, 2005, which is a national stage application of PCT/EP04/04374, filed April 26, 2004. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European patent Office on April 28, 2003. It is noted, however, that applicant has not filed a certified copy of the 03/04491 application as required by 35 U.S.C. 119(b).

### ***Specification***

3. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

### **Arrangement of the Specification**

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in

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upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
  - (1) Field of the Invention.
  - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

### ***Claim Objections***

5. Claims 1-5, 11, and 12 are objected to because of the following informalities:

Claims 1-5, 11, and 12 are objected to for containing non-elected subject matter within the claims. Appropriate correction is required.

6. Claim 1 contains at the end, the phrase, "...or optically pure enantiomers, mixtures of enantiomers, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixture of diastereoisomeric

racemates, or meso forms, or pharmaceutically acceptable salts thereof.” This is not proper because it does not agree in number with “A compound” and therefore is indefinite. Examiner suggests rewriting the claim to read, “...or an optically pure enantiomer, a mixture of enantiomers, a racemate, an optically pure diastereoisomer, a mixtures of diastereoisomers, a diastereoisomeric racemate, a mixture of a diastereoisomeric racemate, a meso form, or a pharmaceutically acceptable salt thereof.” ” Appropriate correction is required.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-3, 5, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound or composition where R<sup>1</sup>-R<sup>4</sup> are hydrogen; R<sup>5</sup> is hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, -(CH<sub>2</sub>)<sub>m</sub>-CO<sub>2</sub>-C<sub>1</sub>-C<sub>5</sub> alkyl; -(CH<sub>2</sub>)<sub>m</sub>-C(O)NH<sub>2</sub>; R<sup>6</sup> is hydrogen or alkyl; and n=0, does not reasonably provide enablement for any other compounds or compositions not previously mentioned above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (United States v. Teletronics Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a

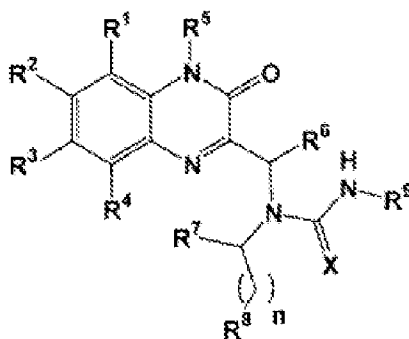
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single factor, but rather a conclusion reached by weighing many factors (See Ex parte Forman 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

These factors include the following:

1) *Amount of guidance provided by Applicant.* Applicant has provided no guidance, examples, or provided any chemical or biological data and/or testing results of any compounds that fall outside of the scope previously mentioned in the current application.

The Applicant has demonstrated within the application how to make a number of quinoxalin-3-one compounds and compositions. Within the application, Claim 1 states a general formula (I):



Applicant has demonstrated the synthesis of a number of compounds, however, they all fall into a much smaller category than that of the broad claim 1. Applicant has only demonstrated compounds that have the following characteristics: R<sup>1</sup>-R<sup>4</sup> are hydrogen; R<sup>5</sup> is hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, -(CH<sub>2</sub>)<sub>m</sub>-CO<sub>2</sub>-C<sub>1</sub>-C<sub>5</sub> alkyl; or -(CH<sub>2</sub>)<sub>m</sub>-C(O)NH<sub>2</sub>; R<sup>6</sup> is hydrogen or alkyl; and n=0. Applicant has not demonstrated any of the tens of thousands of compounds that have been claimed outside of this minute scope.

2) *Unpredictability in the art*. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166.

. Chemistry is unpredictable. See *In Re Marzocchi and Horton* 169 USPQ at 367 paragraph 3:

"Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious). " Dorwald F. A. *Side Reactions in Organic Synthesis*, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

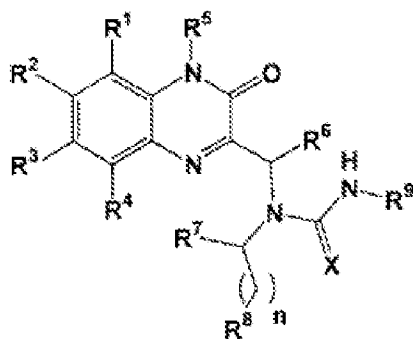
3) *Number of working examples*. The compound core depicted with specific substituents represents a narrow subgenus for which applicant has provided sufficient guidance to make and use; however, this disclosure is not sufficient to allow extrapolation of the limited examples to enable the scope of the compounds instantly claimed or preventive agents. Applicant has provided no working examples of any

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compounds or compositions where the R variables were not those mentioned above in the present application.

“Specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula.” See MPEP 608.01(p).

4) *Scope of the claims.* The scope of the claims involves all the tens of thousands of compounds of the Formula (I):



thus, the scope of the claims is very broad.

5) *Nature of the invention.* The nature of this invention relates to novel quinoxalin-3-one derivatives of the general formula (I) and their use as pharmaceuticals.

6) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a M.S. or Ph.D. degree, and having several years of bench experience.



MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions or treating the diseases mentioned.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "The compound according to Claim 1 selected from the group consisting of:...3-(2-Ethoxy-phenyl)-1-(4-methyl-3-oxo-3,4-dihydro-quinoxalin-2-ylmethyl)-1-((S)-2-phenyl-propyl)-urea;...". There is insufficient antecedent basis for this limitation because claim 1 does not describe a compound or a composition containing this structure even in its broadest sense before the restriction. No new matter is permitted. Appropriate correction is required.

***Conclusion***

11. Claims 1-5, 11, and 12 are rejected.

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12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a US PTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/  
Examiner, Art Unit 1624

**/James O. Wilson/  
Supervisory Patent Examiner, Art Unit 1624**